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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/880,253	06/13/2001	Joseph Attila Rothnagel	13711	7342

7590 12/04/2003

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EXAMINER	
MCKELVEY, TERRY ALAN	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 12/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/880,253	ROTHNAGEL ET AL.	
	Examiner	Art Unit	
	Terry A. McKelvey	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/4/03, 6/11/03, 9/14/03*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,22-25,32-35 and 42-99* is/are pending in the application.

4a) Of the above claim(s) *2,22-25,33,34,44,52-74,76,80,88,92,93,97 and 99* is/are withdrawn from consideration

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-7,32,35,42,43,45-51,75,77-79,81-87,89-91,94-96 and 98* is/are rejected.

7)☒ Claim(s) *81* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10/19, 8/1* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II, claims 1, 3-5, 7, 32, 35, 42-43, 45-51, 75, 77-79, 81-87, 89-91, 94-96, and 98 in the papers filed 3/4/03 and 6/11/03 is acknowledged. The traversal is on the ground(s) that restriction is only appropriate where inventions are independent and distinct, and that all of the groups are different aspects of a single invention and thus are related to each other. It is also argued that certain groups are linked under a single inventive concept, that there is public interest in claiming several aspects of the invention together, reliance on separate classification does not establish independence and distinctness, classification is a poor basis for requiring restriction, continued increase of fees and impact on applicant resources, vital that the restriction requirements issue with only the proper statutory authorization, and that a determination to make the pending restriction requirement final must evidence the patentable distinctness of all defined fifteen groups, one from the other, as presented. This is not found persuasive because of the following reasons.

Concerning the applicants' interpretation of 35 U.S.C. § 121 that both independence and distinctness be present for

restriction between two inventions to be proper, the law has long been established that dependent inventions may be properly divided if they are in fact "distinct" inventions. See M.P.E.P. § 802.01. The Courts have interpreted the statute to mean "or" instead of "and" in 35 U.S.C. § 121.

The allegations that the inventions are "related" to each other and are linked under a single inventive concept is not persuasive that the restriction is not proper because distinct inventions are related, but they are still distinct. The specific reasons set forth for the distinctness (or unrelatedness, which is another way of saying independence) of the inventions were not addressed by the applicant. For example, adding an ATG sequence (which is done in the art at many different sites and for many different reasons) is distinct from removing an GTG sequence (which there are also reasons in the art to do). Identifying art concerning one invention would not necessarily result in the identification of the art of the other, let alone the other 13 inventions. The inventions are distinct such that each invention would require separate searches to do a complete search and examination. As shown by the art rejections below, art has been identified which anticipates and/or renders obvious some claims corresponding to the elected invention. This art, which was identified after a

lengthy and time-consuming search, would not necessarily be applicable to the other inventions.

The argument concerning the public interest in claiming several aspects of an invention together is not persuasive because there are fifteen inventions in the claims, not one. There is also a public and Patent Office interest in examining only one invention per application because requiring examination of more than one invention in an application would either require much higher fees to cover the much higher use of Patent Office resources, which would not be in the interest of inventors who apply for a patent to one invention, or in the absence of higher fees, it would result in a less than complete search and examination for all of the inventions given the extremely limited time given for examination of a given application (which is tied to the existing fee structure), which is also not in the public or Patent Office interest.

The arguments concerning classification are not persuasive because classification is not used for determining independence or distinctness; it is only used for showing burden, which is the other part of the standard for restriction between inventions. Classification is one way of showing that different products and/or methods are sufficiently different that they require different searches, which is the ultimate reason for the

burden in searching and examining independent and/or distinct inventions together, thus requiring restriction.

The argument concerning increase of fees and applicant cost and financial resources is not persuasive because applicant is attempting to apply for a patent to fifteen inventions and must be charged accordingly in order for the inventions to be searched and examined. The Patent Office is fully fee-funded and must recover the costs of searching and examination by charging fees. The system is set up to search and examine one invention per application, and the fee for one invention charged accordingly, with additional continuation and divisional applications being necessary in order to get additional inventions be searched and examined. The examiner has no authority to change the fees and/or the policy that one invention be examined per application; he is simply charged with doing a good job searching and examining a certain number of cases per hours worked. The applicant's elected invention is complex and required a long and difficult search, taking up even more time than is usually allocated for an application. Given the very limited time for an application, it is simply impossible to examine another invention in the instant application, let alone all fourteen additional inventions.

Regarding the argument concerning proper restriction authority, this argument is not persuasive because there is no persuasive argument that there was an improper restriction between the fifteen inventions.

The restriction set forth in the prior communication did set forth the reasons for distinctness and/or independence (indicated as unrelated) for each group, one from the other.

Because the restriction to a single sequence was only applicable to base claims that have been found to be free of the art, the restriction to the single sequence has been withdrawn and the claims drawn to the additional sequences as they apply to the base claims found free of the art are rejoined.

The requirement is still deemed proper and is therefore made FINAL.

It should also be noted that claim 33 was erroneously indicated by the examiner as a part of Group II. It is actually a part of Group I because it is drawn to the removal of ATG. Claim 93 has been amended to only depend on claim 88, which belongs to another group.

Claims 2, 22-25, 33-34, 44, 52-74, 76, 80, 88, 92, 97, and 99 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being

no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the papers filed 3/4/03, 6/11/03, and 9/15/03.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because: Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

There is a non-initialed and non-dated alteration to the address of one inventor.

Claim Objections

Claim 43 is objected to because of the following informalities: the claim does not end in a period as required. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-5, 7, 35, 42-43, 45-51, 96, and 98 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 42, 96, and 98, the use of "[y1y2y3]" renders the claims vague and indefinite because there is no positive antecedent basis for the term; the closest is "{y1y2y3}", but it is unclear whether this term is the intended one.

Also, the use of "comprising altering the nucleotide triplets ... to introduce ... an RTG or RUG to thereby respectively decrease ... the level of expression" renders the claims vague and indefinite because it is unclear how altering the nucleotide triplets will introduce an RTG or RUG. The structure set forth in the claims already have three RTG or RUG triplets. Is the phrase intended to mean that a fourth RTG or RUG triplet is introduced, or is it intended to mean that the resulting structure will have the three RTG or RUG triplets?

Regarding claims 46, etc, the use of "derived from the GLI1 gene leader sequence" renders the claims vague and indefinite because the metes and bounds of what sequences are considered to be derivatives of the GLI1 gene leader sequence are unclear.

Are any changes to the sequence considered to be derivative, or is it intended to mean that the sequence is isolated from the leader sequence (without any internal sequence changes)?

Regarding claims 47, etc, the use of "low stringency conditions" renders the claims vague and indefinite because there is no art-recognized clear definition of the phrase and the specification only indicates what those conditions include, without actually defining the metes and bounds delineating what is not included.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4-5, 32, 87, 89-91, and 94-95 are rejected under 35 U.S.C. 102(b) as being anticipated by Reff (U.S. Patent No. 5,648,267).

Reff teaches to translationally impair the selectable marker of an expression vector, in order to improve the efficiency of protein expression (of the heterologous gene to be

expressed by the vector in addition to the selectable marker) by significantly decreasing the number of viable colonies (column 3). This reference teaches creating a translationally impaired selectable marker gene by adding an ATG triplet upstream of the authentic ATG start site of the neo gene (claim 1; Figure 1). The intent of the added start codon is to, in effect, further impair translation of the selectable marker (column 12). This reference teaches that the cell line is preferably of mammalian origin (but does not exclude other eukaryotic cell lines), and specifically teaches human cell lines (column 15).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered

therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4-5, 32, 75, 77-79, 87, 89-91, and 94-95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reff (U.S. Patent No. 5,648,267) in view of Haselkorn et al (U.S. Patent No. 6,306,636 B1).

Reff teaches to translationally impair the selectable marker of an expression vector, in order to improve the efficiency of protein expression (of the heterologous gene to be expressed by the vector in addition to the selectable marker) by significantly decreasing the number of viable colonies (column 3). This reference teaches creating a translationally impaired selectable marker gene by adding an ATG triplet upstream of the authentic ATG start site of the neo gene (claim 1; Figure 1). The intent of the added start codon is to, in effect, further impair translation of the selectable marker (column 12). This reference teaches that the cell line is preferably of mammalian

origin (but does not exclude other eukaryotic cell lines), and specifically teaches human cell lines (column 15).

Reff does not specifically teach translationally impairing a gene in plant cells.

Haselkorn et al teach that the upstream AUG codons (referring to the mRNA encoded by the gene, which is ATG in the gene itself) are believed to affect the efficiency of mRNA translation and as such may be important in the regulation of expression of some genes. They are also found in some plant mRNAs (column 37).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the translational impairing method taught by Reff by substituting the animal cells taught by Reff with plant cells because Haselkorn et al teaches that AUGs (corresponding to ATGs in the DNA) upstream of the start site affect translation, including in plants, and Reff teaches the general utility of translationally impairing selectable markers in order to increase expression of the other heterologous gene in the vector.

One would have been motivated to do so for the expected benefit of increasing the expression of heterologous genes in plant cells as taught by the combination of the cited references. Based upon the teachings of the cited references,

the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 1, 4-5, 32, 75, 77-79, 82-87, 89-91, and 94-95 rejected under 35 U.S.C. 103(a) as being unpatentable over Reff and Haselkorn et al as applied to claims 1, 4-5, 32, 75, 77-79, 87, 89-91, and 94-95 above, and further in view of Engler et al (U.S. Patent No. 5,262,316) and Hansen et al (U.S. Patent No. 6,051,409).

Reff and Haselkorn et al are taught above and applied as before.

Reff and Haselkorn et al do not specifically teach the plant cell being from cotton or a cereal crop, or the target sequence whose expression is modulated confers resistance to a herbicide or pesticide.

Engler et al teaches transformation of plant cells and that exogneous genes to be introduced into plant cells include selectable plant marker genes to permit screening and selection of transformed cells and functional genes to be introduced and expressed in plants may be a structural gene which encodes a polypeptide which imparts the desired phenotype, including herbicide resistance, pesticide resistance, etc (columns 5-6).

Hansen et al teach that plants can be transformed with any desired DNA fragment which the skilled artisan desires to have integrated into the cell genome such as one that expresses a protein of interest (column 12). The DNA fragment comprises appropriate regulatory sequences, including the leader sequence, which direct the expression of the gene in the DNA fragment (column 9). This reference teaches that the potential plant targets includes cotton and cereal plants (column 12).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method made obvious by the combined teachings of Reff and Haselhorn et al as taught above by using as the plant cells cereal crop or cotton cells as taught by Hansen et al or to use as the target sequence to be modulated a herbicide or pesticide resistance gene as taught by Engler et al because both Engler et al and Hansen et al teach that it is within the ordinary skill in the art to transform plant cells with an expressed gene encoding a desirable trait, Engler et al teach that the desirable trait can be herbicide or pesticide resistance gene, and Hansen et al teach that the plant cells can be cotton or a cereal crop.

One would have been motivated to do so for the expected benefit of making plant cells that more efficiently express a heterologous gene as taught by Reff, in plants as taught by the

other cited references. One would have been specifically motivated to use the cells from specific crops because these are taught as target plants by Hansen et al, which are economically important. One would have been motivated to specifically reduce the resistance genes taught by Engler et al in order to reduce the expression of these genes to just the level needed for the desired resistance. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Allowable Subject Matter

Claim 81 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Conclusion

No claims are allowed.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December

28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is 703-872-9306. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning rejections or other major issues in this communication or earlier communications from the examiner should be directed to Terry A. McKelvey whose telephone number is (703) 305-7213 until January 14, 2004, and (571) 272-0775 after January 14, 2004. The examiner can normally be reached on Monday through Friday, except for Wednesdays, from about 7:30 AM to about 6:00 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to his office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached on (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Terry A. McKelvey, Ph.D.
Primary Examiner
Art Unit 1636

December 1, 2003